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# o-Cresol

CAS #95-48-7

Swiss CD-1 mice, at 0.0, .05, 0.2, and 0.5% in feed

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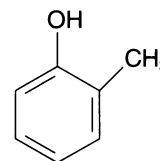
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o-Cresol (OC) is widely used as a disinfectant, solvent, oil additive, component of creosote, and finds its way into air and water from various combustion processes. In previous 90-day prechronic toxicity study, murine estrous cycle was lengthened after exposure to OC. Because of the preliminary indications of toxicity and the relative paucity of public access information, OC was tested for its effects on reproduction and fertility in Swiss CD-1 mice using the RACB protocol. A 2-week dose-range-finding study (Task 1) used feed concentrations of 0.2 to 3% in feed. At 1% OC and above, adverse clinical signs appeared and weight loss was apparent. Mortality was significant at the 3% level. Thus, exposure concentrations for the Task 2 continuous cohabitation study were set at 0.05, 0.2, and 0.5% in feed. Based on mean feed consumption and body weight, the estimated dosages during Task 2 were approximately 60, 220, and 550 mg/kg/day.

No mice died during Task 2. Fertility indices were unaffected by OC exposure. Postpartum dam weights were also unaffected, although the cumulative days to deliver the last litter were 2 to 3 days longer for all treated groups versus controls. However, there was no relationship to dose and no worsening of this "effect" over time, making the biological importance of this suspect.

The last litter was nursed by the dam until weaning. Pup survival and body weights were unaffected to postnatal day 21, as was dam weight and food or water consumption.

Because no reproductive effects were detected in Task 2, no crossover test (Task 3) was necessary. Thus, after the weaning of the  $F_1$  mice, a limited necropsy was conducted on the  $F_0$  adults. For males, there were no effects on body or organ weights, or on sperm indices. The same is true for females: no effects on body or

organ weights. There were no microscopic lesions associated with OC exposure.

The fertility of only the control and high dose  $F_1$  mice was evaluated in Task 4. The only notable effect was a approximately 4% reduction in adjusted pup body weight; all other indices were unchanged.

A necropsy was performed on the  $F_1$  adults. There were no changes in male body or organ weights, nor were any sperm end points affected. Females consuming 0.5% OC weighed 5% less than controls, but organ weights were unchanged, as was the estrous cycle. No significant microscopic lesions were noted in treated animals.

Thus, mild effects on body weight and pup weight were found in the second-generation mating trial. The only conclusions that can be drawn about the relative reproductive toxicity of OC is that ortho-cresol was not toxic at the doses and route used in this study.

**Summary:** NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB92176890

Chemical: o-Cresol

CAS#: 95-48-7

Mode of exposure: Feed

Species/strain: Swiss CD-1 mice

F <sub>0</sub> generation	Dose concentration →	0.05%	0.2%	0.5%
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	—, —
Kidney weight <sup>a</sup>		•	•	—, —
Liver weight <sup>a</sup>		•	•	—, —
Mortality		—, —	—, —	—, —
Feed consumption		—, —	—, —	—, —
Water consumption		—, —	—, —	—, —
Clinical signs		—, —	—, —	—, —

Reproductive toxicity			
̄x litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Cumulative days to litter	↑	↑	↑
Absolute testis, epididymis weight <sup>a</sup>	—, •	—, •	—, •
Sex accessory gland weight <sup>a</sup> (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•, •, •	•, •, •	•, •, •
Estrous cycle length	—	—	—

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F <sub>1</sub> generation	Dose concentration →	0.05%	0.2%	0.5%
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		—, —	—, —	—, —
Mortality		—, —	—, —	—, —
Adult body weight		•	•	—, ↓
Kidney weight <sup>a</sup>		•	•	—, —
Liver weight <sup>a</sup>		•	•	—, —
Feed consumption		•	•	—, —
Water consumption		•	•	—, —
Clinical signs		—, —	—, —	—, —

Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	—, ↓
Absolute testis, epididymis weight <sup>a</sup>	•	•	—, —
Sex accessory gland weight <sup>a</sup> (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	—

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	0.02%
NOAEL general toxicity:	0.2%
F <sub>1</sub> more sensitive than F <sub>0</sub> ?	No
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. <sup>a</sup>Adjusted for body weight.